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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,159	11/05/2001	Timothy W. Lovenberg	ORT-1528	8725

7590 10/01/2004

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)
	09/993,159	LOVENBERG ET AL.
	Examiner	Art Unit
	Michael C. Wilson	1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 August 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *18 August 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attached Response to Arguments*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-7*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☒ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). *8-8-03*.

10. ☐ Other: _____

Response to Arguments

101/Utility

Applicants argue the claimed mice have utility because "integra LifeSciences I Ltd. v. Merck KGaA, 66 U.S.P.Q.2d 1865 (Fed. Cir. 2003) found knockout mice to have value in the industy. Applicants' argument is not persuasive. The case relates to the RGD peptide and discusses using nude mice, arthritic mice and mice with artificially induced vascularization. "Integra LifeSciences" does not mention knockout mice. Knockout mice can have utility; however, in this case, the specification does not teach how to use a mouse having the disruption in an H3 receptor gene that is insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse as a model of any disease or to identify compounds capable of treating disease. Using the mice to "further research" the role of H3 receptors in various diseases is not credible, substantial or significant. An H3 receptor gene disruption has not been linked to any disease condtion (no credible or substantial utility). No drugs relating to treating insensitivity to amnesic effects of scopolamine as claimed have been found (no credible or substantial utility). Determining the role of the H3 receptor in disease is not a substantial utility because a disruption in an H3 receptor gene may not cause disease.

Applicants argue Toyota found a use for mice with a disruption in the histamine H3 receptor gene as claimed; therefore, the mice have utility. Applicants' argument is not persuasive. Toyota was not available at the time of filing. The only utility described by Toyota is "further research", i.e. to determine the role of the protein in "peripheral and

CNS functions or to to detemine the pathophysiological states associated with altered histaminergic activity", which is not a substantial utility because those properties may not exist. More specifically, the specification as originally filed did not teach or suggest using the mice claimed to study the role or H3 receptors in peripheral and CNS functions, etc. as described by Toyota.

Applicants point to Durant (WO95/11894) and argue the claims have utility because Durant described an antagonist of H3 receptor that can be used to treat Alzheimers. Applicants' argument is not persuasive. Using the antagonist to treat Alzheimers as suggested in col. 4, lines 16-24, is not substantial because the H3 receptor has not been linked to Alzheimers, because the drug has not been used since to treat Alzheimers and because Durant did not teach treating Alzheimers patients with the drug. In addition, the claims require a mouse that is insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse which is not described by Durant. The mouse that is insensitive to amnesic effects of scopolamine does not correlate to a mouse that has Alzheimers. The specification does not enable one of skill to use the mouse having the phenotype to determine drugs capable of treating Alzheimers or any other disease.

Applicants argue Perez-Garcia taught the effects of H3 recpetor ligands. Therefore, applicants conclude the mice claimed have a utility. Applicants' argument is not persuasive. Perez-Garcia does not teach any ligands of H3 receptor that treat disease. In fact, Perez-Garcia taught "neither the psychopharmacology of histamine H3 receptors not the therapeutic value of their ligands is clear enough." (pg 216, col. 1,

lines 3-5). Perez-Garcia does not teach how to use mice that are insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse as claimed.

Applicants argue H3 receptor has been linked to cholinergic regulation of memory and cognitive processes as described on pg 10, lines 1-2, of the specification. Therefore, applicants conclude the mice claimed have a utility. Applicants argument is not persuasive. The claims do not require the mice have a deficit in cholinergic regulation of memory or cognitive processes. Mice with a deficit in cholinergic regulation of memory or cognitive processes do not correlate to mice that are insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse. In addition, the specification does not teach how to use mice with a deficit in cholinergic regulation of memory or cognitive processes.

112/1st Enablement

Enablement regarding the use of the mice claimed has not been specifically addressed in applicants arguments.

Applicants argue the claims are enabled for any disruption in the histamine H3 receptor gene to make mice that are insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse. Applicants argument is not persuasive. The claims are not limited to a "total absence of H3 receptors" as described on pg 9, lines 10-15, of the specification. The claims are not limited to a mouse with a homozygous disruption as described in Fig. 1 and 2 having

the phenotype claimed. The specification does not teach which of the two H3 receptors described by West of record were disrupted or that any disruption in any H3 receptor will result in the phenotype claimed. In addition, Takahashi (Dec. 2002, J. Clin. Investig., Vol. 110, pg 1791-1799) taught a mouse with a different disruption of the histamine H3 receptor gene was obese. Thus, different disruptions cause different phenotypes.

112/2nd Indefiniteness

Applicants' arguments regarding the 112/2nd indefiniteness rejections are moot because the rejections were withdrawn in the office action of 5-18-04.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER